

DEPARTMENT OF HEALTH AND HUMAN SERVICES
NATIONAL INSTITUTES OF HEALTH

Fiscal Year 2004 Budget Request

Witness appearing before the
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Mr. Chairman and Members of the Committee, I am pleased to present the President's budget request for the AIDS research programs of the NIH for Fiscal Year 2004, a sum of \$2,869,858,000 an increase of \$122,395,000 above the comparable FY 2003 appropriation.

The NIH represents the largest and most significant public investment in AIDS research in the world. It supports a comprehensive program of basic, clinical, and behavioral research on HIV infection and its associated opportunistic infections and malignancies that will lead to a better understanding of the basic biology of HIV, the development of effective therapies to treat it, and the design of better interventions to prevent new infections. Perhaps no other disease so thoroughly transcends every area of clinical medicine and scientific investigation, crossing the boundaries of the NIH institutes. The Office of AIDS Research (OAR) plays a unique role at the NIH. OAR coordinates the scientific, budgetary, and policy elements of the NIH AIDS program, supported by nearly every Institute and Center; prepares an annual comprehensive trans-NIH plan and budget for all NIH-sponsored AIDS research; facilitates NIH involvement in international AIDS research activities; and identifies and facilitates scientific programs for multi-institute participation in priority areas of research.

THE WORLDWIDE PANDEMIC

HIV has already infected more than 60 million people around the world. According to a new CIA report, "The HIV/AIDS pandemic continues to spread around the world at an alarming rate, and the number of people with the disease will grow significantly by the end of the decade, as it becomes more geographically diffuse. By 2010, we estimate that five countries of strategic importance to the United States – Nigeria, Ethiopia, Russia, India, and China – collectively will have the largest number of HIV/AIDS cases on earth." A recent article in *Foreign Affairs* magazine stated, "The spread of HIV/AIDS through Eurasia, in short, will assuredly qualify as a humanitarian tragedy – but it will be much more than that. The pandemic there stands to affect, and

alter, the economic potential – and by extension, the military power – of the region’s major states ... Over the decades ahead, in other words, HIV/AIDS is set to be a factor in the very balance of power within Eurasia – and thus in the relationship between Eurasian states and the rest of the world.” Dramatic increases in HIV infection also are occurring in Eastern Europe, Central Asia, Latin America, and the Caribbean. An article in the *New York Times* recently reported another dimension to the epidemic: “As a result of HIV, the worst-hit African countries have undergone a social breakdown that is now reaching a new level: African societies’ capacity to resist famine is fast eroding. Hunger and disease have begun reinforcing each other.”

THE U.S. EPIDEMIC

The Centers for Disease Control and Prevention (CDC) recently reported that more people were diagnosed with AIDS in 2001, the latest year for which reliable statistics are available, than the previous year, or any year since 1998. After years of sharp declines, thanks largely to successful treatment with new antiretroviral therapies (ART), this report indicates a reversal in cases of AIDS in the U.S. Further, CDC reported that the rate of new HIV diagnoses, which had remained stable since 1990, also appears to be increasing. New HIV infections rose a striking 8 percent between 1999 and 2001, based on data from 25 states with mandatory HIV reporting, which does not include the two highest prevalence states of New York and California. HIV infection rates continue to climb among women, racial and ethnic minorities, young homosexual men, individuals with addictive disorders, and people over 50 years of age. In addition, use of ART has now been associated with a series of side effects and long-term complications that may have a negative impact on mortality rates. The appearance of multi-drug resistant strains of HIV presents an additional serious public health concern. According to CDC reports, approximately one quarter of the HIV-infected population in the United States also is infected with Hepatitis C virus (HCV). AIDS affects African Americans and Hispanics disproportionately. According to CDC figures through December 2001, approximately 64 percent of newly infected women

are African American and 17 percent are Hispanic. Among newly infected men, approximately 43 percent are African American and 20 percent are Hispanic. This expanding and evolving U.S. epidemic presents new and complex scientific challenges.

COMPREHENSIVE AIDS RESEARCH PLAN AND BUDGET

To address these compelling scientific questions, the OAR develops an annual comprehensive trans-NIH AIDS research plan and budget, based on the scientific priorities and opportunities that will lead to better therapies and prevention strategies for HIV infection and AIDS. The planning process is inclusive and collaborative, involving the NIH Institutes, as well as eminent non-government experts from academia, industry, foundations, and AIDS community representatives. The Plan serves as the framework for developing the annual AIDS research budget for each Institute and Center, for determining the use of AIDS-designated dollars, and for tracking and monitoring those expenditures.

The Plan establishes the NIH AIDS scientific agenda in the areas of: Natural History and Epidemiology; Etiology and Pathogenesis; Therapeutics; Vaccines; and Behavioral and Social Science. In addition, the plan addresses the cross-cutting areas of: Microbicides; Racial and Ethnic Minorities; Women and Girls; Prevention Science; International Research; Training, Infrastructure, and Capacity Building; and Information Dissemination. In consultation with the Director of NIH, the OAR determines the total annual AIDS research budget. Within that total, the OAR establishes the AIDS research budgets for each NIH Institute and Center, in accordance with the priorities and objectives of the Plan, at each step of the budget development process up to the Conference Committee. To accomplish this, OAR consults regularly with the Institute and Center Directors. This process allows the OAR to ensure that NIH AIDS research funds will be provided to the most compelling scientific opportunities, rather than a distribution based solely on a formula.

OAR plays a crucial role in identifying scientific areas that require focused attention and facilitating multi-Institute activities to address those needs. OAR fosters this research through a number of mechanisms, such as designating funds and supplements to jump-start or pilot program areas, sponsoring workshops or conferences to highlight a particular research topic, and sponsoring reviews or evaluations of research program areas to identify research needs.

The overarching priorities that continue to frame the NIH AIDS research agenda are: prevention research to reduce HIV transmission, including development of vaccines, microbicides, and behavioral interventions; therapeutics research to develop simpler, less toxic, and cheaper drugs and drug regimens to treat HIV infection and its associated illnesses, malignancies, and other complications; international research, particularly to address the critical needs in developing countries; and research targeting the disproportionate impact of AIDS on minority populations in the United States. All of these efforts require a strong foundation of basic science, the bedrock of our research endeavor.

NEW CHALLENGES IN THERAPEUTICS RESEARCH

While multiple ART drug combinations continue to successfully reduce viral load and restore immune responses in many HIV-infected individuals, these regimens also can result in serious toxicities and side effects, single- and multiple drug-resistance, and other complications which make them unacceptable for some individuals. These side effects and complications appear to be increasing as HIV-infected individuals continue on drug regimens. More deaths occurring from liver failure, kidney disease, and cardiovascular complications are being observed in this patient population. NIH-sponsored research efforts continue to develop better antiretroviral drugs and treatment regimens that demonstrate less toxicity, activity in viral and cellular reservoirs, reduced development of drug resistant virus, improved pharmacodynamics and pharmacokinetics, easier compliance, and lower cost.

While the incidence of certain opportunistic infections (OIs) and malignancies has decreased with the advent of ART, the number of cases of TB, multiple drug resistant TB, and other coinfections such as Hepatitis B virus and Hepatitis C virus has increased. The development of practical and affordable treatment regimens against HIV coinfections and endemic diseases in developed and developing nations is an NIH priority.

PREVENTION RESEARCH

NIH supports a comprehensive approach to HIV prevention research that includes contributions from the biomedical, behavioral, and social sciences. Our biomedical prevention research priorities include the development of vaccines, topical microbicides, strategies to prevent mother-to-child transmission—including a better understanding of risk associated with breast-feeding—and management of sexually transmitted diseases (STDs). NIH also supports behavioral research strategies, including interventions related to drug and alcohol use. Efforts continue to identify the most appropriate intervention strategies for different populations and sub-epidemics in the U.S. and around the world. As a result of increased NIH funding, many new approaches to HIV vaccines are being pursued. Although production of candidate vaccines for clinical study has proceeded slowly, at least 10 new candidate vaccines will enter Phase I trials in the next 2 years. Several new combinations of products, which are expected to provide better immune responses, also will be tested in Phase I or II trials. The Dale and Betty Bumpers Vaccine Research Center, located on the NIH campus, recently launched the first Phase I clinical trial of a multi-clade, multi-gene vaccine candidate.

INTERNATIONAL RESEARCH

To address the increasing urgency of the AIDS pandemic, the OAR established an initiative and strategic plan for global research on HIV/AIDS and has significantly increased research efforts in the past several years to benefit resource- and

infrastructure-poor nations. NIH supports a growing portfolio of research conducted in collaboration with investigators in developing countries. Results of this research benefit the people in the country where the research is conducted, as well as people affected by HIV/AIDS worldwide. Critical to the success of these international studies are foreign scientists who are full and equal partners in the design and conduct of collaborative studies. To that end, NIH also supports international training programs and initiatives that help build infrastructure and laboratory capacity in developing countries where the research is conducted.

WOMEN AND MINORITIES

Women experience HIV/AIDS differently from men. NIH research has demonstrated that women progress to AIDS at lower viral load levels and higher CD4 counts than men. Women also experience different clinical manifestations and complications of HIV disease. These findings may have implications for care and treatment of HIV-infected women, particularly with ART. There are many research questions that remain unanswered about specific characteristics of women and girls that might play a role in transmission, acquisition, or resistance to HIV infection during different stages of the life course.

In many U.S. urban centers, HIV seroprevalence rates mimic those found in some developing nations. These findings, along with the resurgence of STDs and associated high-risk behaviors, demonstrate the need for comprehensive strategies to decrease HIV transmission in affected vulnerable populations, and improve treatment options and treatment outcomes. OAR is directing increased resources toward research to develop new interventions that will have significant impact on these groups. These include interventions that address the co-occurrence of other STDs, hepatitis, drug abuse, and mental illness; and interventions that consider the role of culture, family, and other social factors in the transmission and prevention of these disorders in minority communities. NIH is making significant investments to improve research infrastructure

and training opportunities for minorities and will continue to ensure the participation of minorities in AIDS clinical trials, as well as in natural history, epidemiologic, and prevention studies. OAR has provided additional funds to projects aimed at increasing the number of minority investigators conducting behavioral and clinical research; targeting the links between substance abuse, sexual behaviors, and HIV infection; increasing outreach education programs targeting minority physicians and at-risk populations; and expanding the portfolio of population-based research. One of these projects is a series of Training and Career Development Workshops that provide minority investigators with an opportunity to learn more about available NIH funding mechanisms and to meet and network with senior minority investigators who receive significant levels of NIH funding.

SUMMARY

The human and economic toll of the AIDS pandemic is profound. It requires a unique response that is complex, comprehensive, multi-disciplinary, and global. The NIH role in this response is fundamental and unprecedented. The diverse AIDS research portfolio demands scientific coordination and management of research funds to enhance collaboration, minimize duplication, and ensure that precious research dollars are invested in the highest priority areas of scientific opportunity. The nation's investment in AIDS research is reaping even greater dividends, as AIDS research is unraveling the mysteries surrounding many other infectious, malignant, neurologic, autoimmune, and metabolic diseases.

The authorities of the Office of AIDS Research allow NIH to pursue a united research front against the global AIDS epidemic. We are deeply grateful for the continued support this Committee has provided to our efforts.